





Ramazan Serdar Arslan^{1*}, Erdem Obuz², Yamac Erhan³, Elvan Erhan⁴, Hasan Aydede³ and Eray Kara³

¹Department of General Surgery, Banaz State Hospital, 64520, Banaz, Usak, Turkey. ²Department of General Surgery, Esme State Hospital, 64600, Esme, Usak, Turkey. ³Department of General Surgery, Faculty of Medicine, Celal Bayar University, 45030, Manisa, Turkey. ⁴Department of Algology, Faculty of Medicine, Ege University, 35100, İzmir, Turkey.

Authors' contributions

This work was carried out in collaboration between all authors. Author RSA designed the study, wrote the protocol and wrote the first draft of the manuscript. Author EO performed the statistical analysis. Authors YE and EE managed the analyses of the study. Authors HA and EK managed the literature searches. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Objectives: Persistent pain and sensory disturbances following surgical treatment for breast cancer is a significant clinical problem. The goal of this study was to investigate the incidence and clinical characteristics of persistent postmastectomy pain (PPMP) and its impact on quality of life. **Methods:** Between 1998 and 2013, one hundred thirty-five patients who had undergone a mastectomy operation for breast cancer by the same surgeons were evaluated. Patients who had more than one operation or died during follow up were excluded. All patients were contacted by telephone and were questioned about the presence of PPMP. Patients who had PPMP were

*Corresponding author: Email: r.serdar.arslan@gmail.com, r.arslan@saglik.gov.tr;

invited for face to face interview and assessed with a Pain Questionnaire Form and LANSS Pain Scale.

Results: 99 out of 135 patients (73.3%) were contacted by telephone. The incidence of PPMP was 16.2%. Pain Questionnaire revealed that 50% of the patients had mild pain, 37.5% had moderate pain, and 12.5% had severe pain. The rate of neuropathic pain symptoms varied between 25% and 81%. According to LANSS Pain Scale, neuropathic mechanisms were likely to be contributing to the patient's pain in 56% of the patients. 56% of the patients with pain needed analgesia, 12.5% reported that their pain was their worst medical problem limiting their daily activities. **Conclusion:** The incidence of PPMP was 16.2% and the contribution of neuropathic mechanisms

was 56% in our study. About 50% of the patients with PPMP had moderate to severe pain necessitating analgesia.

Keywords: Postmastectomy; pain; LANSS; scale; mastectomy; chronic.

ABBREVIATIONS

- *PPMP* : *Persistent postmastectomy pain*
- CPCP : Chronic postsurgical pain
- BCS : Breast conserving surgery
- SLNB : Sentinel lymph node biopsy
- SM : Simple mastectomy
- MRM : Modified radical mastectomy
- AD : Axillary dissection
- LANSS : Leeds assessment of neuropathic symptoms and signs

1. INTRODUCTION

Breast cancer is the most common type of cancer in women in Turkey and in the United States [1]. Breast cancer is the most lethal cancer type after lung cancer in women [1]. With the early diagnosis and treatment of breast cancer, the life expectancy of the patients is prolonged but the biological, physiological and psychological morbidities are emerging in the patients [2,3]. Chronic postsurgical pain (CPSP) is considered to be a clinical condition that is seen after some surgical interventions [4]. The breast cancer surgery is thought to have a significant risk of developing CPSP [4]. Persistent postmastectomy pain (PPMP) is defined as persistent or reoccurring pain in the incision, axillary, inner part of arm and chest wall of the mastectomy at least 2 months after surgical intervention [4]. Although there is very little information about the aetiology of PPMP, it is assessed as a combination of nociceptive and neuropathic pain [5]. During surgery, axillary, chest wall nerves damage and intercostobrachial nerve damage are thought to cause PPMP [5,6]. During mastectomy, the occurrence of damage in intercostals, axillary and intercostobrachial nerves and an inflammatory reaction at the surgical incision site lead to peripheral and central sensitisation in the sensorial system

followed by a pain, hyperalgesia and/or allodynia at the surgical incision site [7,8].

Similar to the characteristics of other chronic pain syndromes, PPMP is described as having burning, stinging and electric shocking effects. It is usually mild or moderate, but may also be severe in a small group of patients [4,11,12,13,14].

LANSS (The Leed assessment of neuropathic symptoms and signs) pain scale, nociceptive with neuropathic pain is a simple but useful test in the differential diagnosis of pain. The pain scale of the LANSS consists of two parts; The first part filled by the patient himself and the doctor the second part with a short physical examination. The patient himself answered five physical examination of the patient's experience with neuropathic pain and whether there is allodynia by touching the painful and painless area with cotton is tested. If the score is 12 and above, it is classified as neuropathic and if it is below twelve, it is classified as nociceptive pain.

The risk of developing PPMP during mastectomy cases is reported to be between 25% and 60% in different studies [9-13]. The type of operation, age of the patient, adjuvant chemotherapy, radiotherapy, psychosocial status, the presence of preoperative pain, and severity of postoperative pain affect the incidence of PPMP [3,6,7,14,15,16].

This study aimed at determining the incidence of PPMP in patients who underwent a mastectomy at the Department of General Surgery, Faculty of Medicine of Celal Bayar University. The impact of pain on daily, the progress, severity and characteristics of PPMP, life and use of analgesics were investigated.

2. MATERIALS AND METHODS

Patients who underwent a mastectomy operation by the same surgeons in between 1 January 1998 and 1 June 2013 were investigated. Patients who underwent more than one operation, who were lost to follow up due to death, were not included in the study. All patients with records of surgical treatment for breast cancer during the course of the study were included in the potential participant pool. The demographical data of patients (age, gender), diagnosis, type of surgical intervention undergone and date of operation were recorded on the basis of the information obtained from patient charts. All the patients included in the study were called September 2013 and those patients who could be reached over the phone were asked if they had any pain associated with the surgical intervention. Patients whose pain started and continued after mastectomy operation were called for interview. Their pain was assessed using a Pain Questionnaire.

Pain Questionnaire Form (Table 1) was used in the evaluation of pain. The impact of pain on daily the progress, severity and characteristics of PPMP, life and use of analgesics were assessed on this questionnaire. Descriptive analyses were performed and results shared.

3. RESULTS

One hundred and thirty five patients who had an operation at the Department of General Surgery of the Faculty of Medicine were examined. Twenty four (17.8%) could not be reached by phone, twelve of them died (8.9%). Ninty-nine patients were included to study (73.3%). Sixteen cases reported that they had pain after breast cancer surgery (Fig. 1). The incidence of PPMP was found to be 16.2%. The demographic data and diagnoses of 99 patients included in the study (with and without pain) are shown in Table 2. All of the 16 patients who reported that you felt the pain came to interview.

The answers obtained from the Pain Questionnaire revealed that 50% of the patients had mild pain intensity, 37.5% had moderate pain severity, and 12.5% had severe pain severity. 87.5% of these patients reported that the patient's pain decreased with time. 56.5% of the patients were using analgesics due to pain, 18.5% were using pain clinic due to pain, 12.5% were the most uncomfortable health problem and 12.5% were restricting the daily activity of the pain reported. When the duration of pain was assessed, the breakdown of 16 patients was found to be 8 patients having pain between 2 months and a year, 4 patients having pain

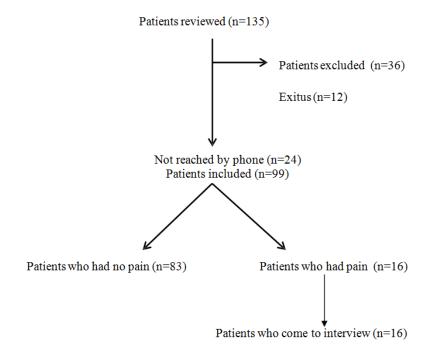


Fig. 1. Patient archive scan steps

Y/N

Table 1. Pain questionnaire

1. Do you suffer with pain due to your breast cancer surgery?

- If patient answer is **Yes** continue completing the rest of the questionnaire
- If **No**: do not complete the rest of the questionnaire (but please return it anyway)
- 2. Which side(s) of your chest was operated on?
- Do you have pain over the scar? Y/N

4. Is your pain felt in the chest wall on the side that was operated on? Y/N

- 5. How long have you had this pain
- 6. Did the pain come on straight after the surgery? Y/N
- 7. Has the pain improved with time? Y/N

8. Do you rate the pain as MILD/MODERATE/SEVERE

9. Are you still receiving treatment or taking medication for the pain? Y/N

- 10. Have you ever attended a specialist Pain Clinic for this pain? Y/N
- 11. Is pain your Worst medical problem? Y/N

12. Does the pain limit your daily activities? Y/N

Think about how the pain has felt over the last week

13. Does your pain feel like strange, unpleasant sensations in your skin? Words like pricking, tingling, pins and needles might describe these sensations. Y/N 14. Does your pain make the skin in the painful area look different from normal? Words like mottled or looking more red or pink might describe the appearance. Y/N 15. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity. Y/N 16. Does your pain come on suddenly and in bursts for no apparent reason when you're still? Words like electric shocks, jumping and bursting describe these sensations. Y/N 17. Does your pain feel as if the skin temperature in the painful area has changed abnormally? Words like hot and burning describe these sensations? Y/N 18. Have you received radiotherapy in the painful region? Y/N 19. Other comments you may have.....

Table 2. Demographic data and diagnoses of 99 patients included in the study

	Pain (+)	Pain (-)
Gender (M / F)	(- / 16)	(1 / 82)
Mean age (min-max)	53 (31-64)	52 (27-77)
Tumor location (Right breast / Left breast)	(11 / 5)	(44 / 39)
BCS + SLNB	-	7
BCS + AD	3	26
MRM	12	50
Radical Mastectomy	1	-

between a year and 2 years, 2 patients having pain between 2 and 3 years and 2 having pain more than 3 years. It was found that 25% of the cases with pain were treated with radiotherapy, 68.5% with chemotherapy and 37.5% with hormonotherapy. When the pain localisations of the patients were examined 37.5% of them were axilla; 56.3% were on the incision and 18.7% were on the arm.

The rate of neuropathic pain symptoms (Questions 13, 14, 15, 16 and 17 in Table 1) varied between 25% and 81.25%. There was prickling, stinging or tingling in 81.25% of the

patients. Nearly 31.25% of the patients described excessive sensitivity to touching. There was burning in 25% of the patients and a sudden exploding pain like an electric shock in 81.25% of them. 37.5% of patients differed in skin appearance.

In addition to questioning the symptoms of neuropathic pain, the pain scores of LANSS were also evaluated, with changes in sensory evaluation of allodynia and pin-prick thresholds [17]. According to this score, 9 out of 16 cases (56.25%) with PPMP were found to score 12.

4. DISCUSSION

The incidence of PPMP in patients who underwent a mastectomy operation at the Department of General Surgery of the Faculty of Medicine was found to be 16.2% in our study. Pain was mild in 68.5% of the patients, moderate in 31.5% of them. There were no patients with severe pain. Our study also revealed that approximately 56.25% of the patients used analgesics for their pain, and 12.5% of them reported that pain was the most disturbing health problem and it restricted their daily activities.

The incidence of PPMP has become the investigated subject of same studies.

The incidence of PPMP in studies is reported to be 25-60%; In our study we found the incidence of PPMP to be lower than 16.2% [9-13]. In general, it is reported that PPMP is mild and moderate in severity but severe pain can be seen in 5% of patients [4].

In previous studies on this subject, Smith et al. [18] submitted a pain questionnaire form to all of the cases in their study of 511 cases that underwent mastectomy for 6 years. The incidence of PPMP in 408 responders was 43%. In this study, the researchers considered the neuropathic pain in the surgical area over three months as a PPMP criterion and reported that the incidence of PPMP (65%) was significantly higher in younger cases (26%) than those older than 70 years. In our study, 56% of cases detected in PPMP were 40 years old or younger; When the age range rose to 45, it was determined that the ratio reached 69%.

Carpenter et al. [19] found 134 cases with mastectomy that they could reach by telephone and found the incidence of PPMP to be 27% in their studies. Kudel et al. [15] also included phantom pain and scarring pain in the postmastectomised study of 274 cases and found it to be as high as 55% of the PPMP incidence.

Steegers et al. [16] found an average of 32% incidence of PPMP. However, according to the applied surgical technique; breast conserving surgery (BCS) + sentinel lymph node biopsy (SLNB) and simple mastectomy (SM) + SLNB patients PPMP incidence 23%; modified radical mastectomy (MRM) and BCS + axillary dissection (AD) pain rate in the patients was 51%. In our study, pain was not detected in 7 cases treated with BCS + SLNB, whereas it was

found as 17.4% (16/92) in patients who underwent AD. Vilholm et al. [20] reported that the PPMP ratio was 7-8% in SLNB treated patients: It is found that the rate of PPMP is increased to 20% in AD patients. Similarly, Poleshuck et al. [21], found the rate of PPMP 61% in AD patients and 31% rate without AD. Fabro et al. [22] found that PPMP was statistically significant when the number of lymph nodes dissected from the axilla was more than 15. The largest series in this topic belongs to of Gartner et al. [23], which was made in Denmark. In the studies they evaluated with the 3253 probability questionnaire, the researchers reported a PPMP of 47%. In the evaluation of painful cases, 48% of the cases had mild pain, 30% had moderate pain, 13% had severe pain, 20% of the patients were treated due to pain. In this study, the fact that patients with ALND were under 40 years of age were shown as factors that increased PPMP risk. There are also differences in analgesic use rates due to PPMP. In the study of Vilholm et al. [20], 38.5% were used, whereas in our study, 56.25% of the patients were using analgesics. Carpenter et al. [19], the use of analgesics was reported as 29%, but due to pain, massage, hot application and presence of vegetative products were reported. Smith et al. [18] found that 21.7 of the patients used analgesics prescribed by physicians, 14.3% of the patients used non-prescription analgesics, 10.9% applied physiotherapy and 2.3% acupuncture.

The localisation of the pain varies between studies. Vilholm et al. [20] showed pain on the incision scar with 55.8%; Arm and axillary are 80,8%. In addition, 75% of the cases reported that the pain was seen in more than one localisation. Stevens et al. [24] found that the PPMP distribution axillary in 84%, in 74% of cases, 58% in chest wall, 32% in the shoulder.

Steegers et al. [16] reported that arm pain (78%) was more common in patients who underwent axillary dissection. Carpenter et al. [19] found that the rate of pain on the incision was 86%, that of axillary was 81% and that of the arm on the same side was 69%. When we evaluated PPMP localisation in our study, axilla 37.5%; 56.25% on the incision and 18.75% on the same side. Similar to most studies, pain localisation has been expressed more than once by patients. In recent studies, Schreiber et al. [25] and Belfer et al. [26] suggested that psychosocial factors are determinant in the development of PPMP. Researchers have stated that depression,

somatisation, anxiety, and thoughts and behaviours are the most important psychosocial factors that increase the risk of PPMP.

The 16.2% PPMP rate we found in our study is lower than other studies, but the different outcomes between studies are influenced by many factors such as pain assessment methods, time to evaluate cases, selected criteria for PPMP definition, type of surgery and patient population. For example, there are some opinions that the incidence of pain may be higher than expected due to the fact that the response rate of the pain cases may be higher in studies conducted by sending the adrese questionnaire form [27]. In our study, cases were contacted by phone and the rate of PPMP was determined by verbal notification of the patient. Patients with pain were also recruited and their pain was questioned in detail, and LANSS scores for neuropathic pain were determined by examining allodynia and hyperalgesia. Unlike prior studies in this regard, the pain of the events in our study was questioned in more detail. LANSS pain scale is a method developed to determine the prevalence of neuropathic mechanisms in pain. LANSS pain scale was used in our study with the questioning of neuropathic pain symptoms (questions 13, 14, 15, 16, 17 in Table 1) and the examination of allodynia and pin-prick threshold values. From a total score of 24. a score ≥12 means that neuropathic mechanisms are likely to be contributing to the patient's pain (LANNS literatür). Accordingly, 56.25% of the patients with PPMP had LANSS pain scores of ≥12 suggesting that neuropathic mechanisms are likely to be contributing to PPMP in our study.

The questioning of neuropathic pain symptoms and the examination of allodynia and pin-prick threshold values are important in revealing the neuropathic component of this pain in patients with PPMP 56.25% of our cases had LANSS pain scores of ≥12. In patients with PPMP, 25% of the symptoms of neuropathic pain 81.25% of the patients, but more than half of the neuropathic pain can be diagnosed. Bruce J et al. [28] reported that psychological factors and intercostobrachial nerve damage were risk factors for the development of PPMP in their new study, young age, axillary dissection and acute postoperative pain severity were determinants of chronic pain. The researchers also found that up to 40% of cases with PPMP had positive neuropathic pain scales.

It is important in the last few days that patients with chronic pain do not have a problem with surgical intervention and that the patient's progress has not been adversely affected by the prognosis. Most of the patients with PPMP are using paramedical methods or taking nonprescription medicines to relieve their aches [19]. Recent posts demonstrate many factors such as the age of the patient, the characteristics of the planned surgical procedure, and the current psychosocial state of the patient affect the incidence of PPMP in cases of mastectomy due to breast cancer.

5. CONCLUSION

PPMP is a health problem that reduces the quality of life of patients.

We believe that minimally invasive surgical interventions to be performed in the early stage of the diagnosis of breast cancer, and psychosocial support for the patients after surgery will decrease the pain rate. Patients with serious pain problems should be followed with the department of algology and psychiatry.

CONSENT AND ETHICAL APPROVAL

As per university standard guideline participant consent and ethical approval has been collected and preserved by the authors.

NOTE

An earlier abstract of this paper was presented at 8 World congress of the World Institute of PAIN (WIP) 2016.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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